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REGULATION OF CALCIUM METABOLISM DURING PROLONGED ANTIORTHOSTATIC HYPOKINESIA

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16. Abstract

Characteristics of the regulation of calcium exchange in healthy persons exposed to 182 days of antiorthostatic hypokinesia are investigated. Total calcium concentrations, ionized calcium activites and parathyroid hormone concetrations in blood serum were determined before, during, and up to 15 days after a 182 day period of strict bed rest at a head-down tilt of 4 deg, and tests of blood u[illegible]e responses to a calcium lactate stress were performed to st[illegible] the role of the kidneys. An increase in calcium ion activity is observed during the period of hypokinesia, while total calcium concentrations changed to a lesser degree. Plasma parathyroid hormone levels are found to significantly exceeed background levels during hypokinesia and in the recovery period immediately following. Finally, the increase in calcium excretion in the urine during prolonged limitations of muscular activity is found to be connected with both an enhancement of calcium filtration and a decrease in its reabsorption in the kidneys, possibly due to changes in hormonal regulation.

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REGULATION OF CALCIUM METABOLISM DURING PROLONGED ANTIORTHOSTATIC HYPOKINESIA

/705*

A. I. Grigor'yev, B. V. Morukov, B. R. Dorokhova and L. A. Rustam'yan

In many publications studying metabolic processes under conditions of hypokinesia, there are indications that prolonged stay of man in bed is accompanied by significant changes in calcium metabolism: increased content of total and ionized calcium in the blood serum [1, 2], increased excretion of calcium by kidneys [3 - 5], decreased absorption of it in the gastrointestinal tract [6, 7], and decreased mineral saturation of the osseous tissue [8, 9]. However genesis of the observed phenomena is still obscure. This work investigates some features in the regulation of calcium metabolism in healthy people under conditions of 182-day antiorthostatic hypokinesia.

Technique

Studies were made with the participation of six essentially healthy volunteer males who spent 182 days in a strict bed mode in an antiorthostatic (-4°) position, and before and after the period of hypokinesia spent 20 days in a normal motor mode under hospital conditions. During the entire observation period, the subjects received a monitored diet which contained 40 - 60 mequi of calcium, 210 - 260 mequi of sodium, 68 - 80 mequi of potassium and 24 - 36 mequi of magnesium.

The concentration of total calcium, the activity of its ionized fraction, as well as the content of parathyroid hormone in the blood serum were studied in the background period, on the 26th, 46th, 86th, 130th and 178th day of the period of hypokinesia, as well as on the 2nd, 6th and 15th day of the period of restoration. During the entire observation period daily release of electrolytes with urine was studied.

The participation of the kidneys in regulating calcium metabolism during prolonged antiorthostatic hypokinesia was studied using a specific

*Numbers in margin indicate pagination in original foreign text.

sample with load by calcium lactate on the background of a 1% maintained water load [10, 11]. The calcium load test was conducted in the background period on the 42nd, 86nd and 166th day of the period of hypokinesia, as well as on the 15th day of the period of restoration.

In the urine and blood samples, the content of calcium and magnesium was studied by the method of atom-absorption spectrophotometry, while the level of sodium and calcium by the method of flame photometry, concentration of creatinine by Popper spectrophotometer. The activity of calcium ions in the serum was measured by the method of direct potentiometry with the help of an ion-selective calcium electrode [12, 13] with t° = 25° and pH = 7.4. Calibration used standard solutions with /706 ion strength equal to the ion strength of blood.

The content of parathyroid hormone in blood plasma of the subject before and after hypokinesia was determined by radio isotope method using standard test set PTH of the firm Cea-Irn-Sorin, the samples were counted on the γ-radiometer (Searle 1175Z). The findings were statistically processed using the dialogue system PRALG/YeS of a computer by mathematical programs developed by V. K. Vasil'yev and L. A. Rustam'yan (Moscow).

Study Results and Their Discussion

The activity of ionized calcium in the blood serum of subjects in the entire period of hypokinesia, as well as on the 2nd and 6th day of the period of restoration significantly exceeded the background level (Figure 1). The concentration of total calcium in the blood was elevated only in the 2nd half of the period of bedrest. The content of parathyroid hormone in the blood plasma of the subjects during the bedrest was considerably higher than under conditions of normal motor activity (see Figure 1) which apparently caused an increase in the content of ionized calcium in the blood serum, since the parathyroid hormone increases the calcium level in the blood mainly because of its ionized fraction [14, 15].

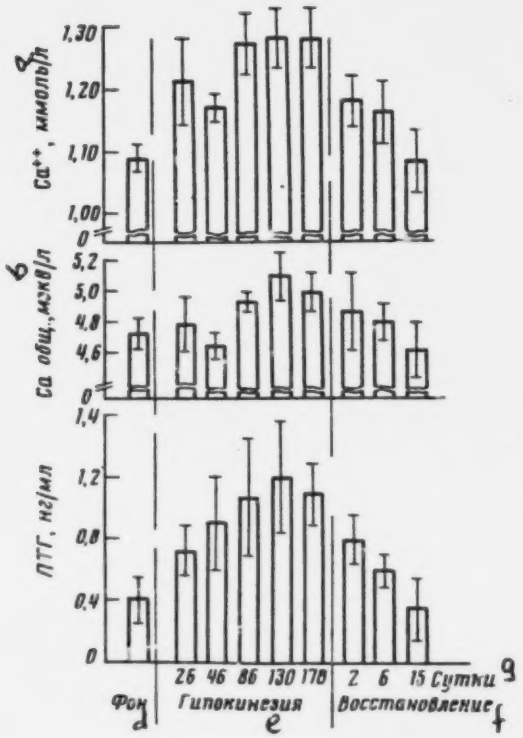

Figure 1. Activity Dynamics of Calcium Ions (Ca^{++}), Concentration of Total Calcium (Ca_o) and Content of Parathyroid Hormone (PTH) in Blood Serum During 182-day Antiorthostatic Hypokinesia and Restoration. (M±mt)

Key:
a. mmole/l
b. mequi/l
c. PTH, ng/ml
d. background
e. hypokinesia
f. restoration
g. days

Daily excretion of calcium with the urine increased starting from the second week of hypokinesia, and during the entire period of stay in bed exceeded the background level. The release of calcium by the /707 kidneys during hypokinesia averaged 3.4 mequi per day higher than with

normal motor activity, which corresponds to the data of balance studies in which losses of calcium by the body both because of increased excretion of it by the kidneys, and because of increased release of calcium with the feces [6 - 7] were taken into consideration. According to these data, the negative calcium balance in the human body with prolonged stay in bed was about 300 mg of Ca per day, and 100 - 150 mg of Ca was lost by the body because of increased release with the urine.

TABLE . RATE OF EXCRETION OF CALCIUM WITH URINE (U_{Ca} x V), CALCIUM CLEARANCE (C_{Ca}) AND EXCRETABLE FRACTION OF CALCIUM (EF_{Ca}) WITH TEST WITH CALCIUM LOAD DURING 182-DAY ANTIORTHOSTATIC HYPOKINESIA (M±m)

1 Показатели	2 Фаза нагрузки	3 Фоновый период	4 Гипокинезия			6 Период восстановления, 15-е сут
			42-е сут 5	82-е сут 5	166-е сут 5	
$U_{Ca} \cdot V$, мкэкв/мин 7	I	7,5±1,4	9,0±1,2	8,7±0,9	7,3±1,6	7,2±1,0
	II	18,5±0,8	22,2±1,5	29,8±1,7	26,0±1,8	19,5±1,7
C_{Ca}, мл/мин 8	I	1,59±0,75	1,95±0,26	1,76±0,18	1,45±0,11	1,55±0,19
	II	3,58±0,41	4,59±0,61	5,80±0,37	4,89±0,2	3,79±0,33
EF_{Ca}, %	I	3,86±0,81	4,10±0,55	3,80±0,43	2,85±0,33	3,4±0 50
	II	8,54±0,45	9,53±0,74	13,32±1,09	10,34±0,40	9,4±3,0

Key:
1. indicators
2. load phase
3. background period
4. hypokinesia
5. day
6. period of restoration
7. μequi/min
8. ml/min

Note: I is the original level (before the load) II is the level during maximum release of calcium.

In conducting the test with calcium load during stay in bed it was found that peroral administration of calcium lactate caused a more

significant increase in the rate of excretion of calcium with the urine, clearance and excretable calcium fraction (table) than under conditions of normal motor activity.

The rate of magnesium excretion in the test with calcium load during hypokinesia was also somewhat higher than in the background period, however the increase in the secretion of calcium was expressed to a considerably greater degree. In conducting the test with calcium load in the background period, the ratio of calcium concentration to magnesium concentration (U_{Ca}/U_{mg}) rose as compared to the original level by 43.2 ± 4.8%. On the 82nd and 166th day of hypokinesia, the U_{Ca}/U_{mg} ratio in the test with calcium lactate load increased by 95.8 ± 8.2 and 83.4 ± 4.9% respectively, thus was significantly ($p < 0.05$) higher than in the background period. The increase in the specificity of the sample for calcium under conditions of hypokinesia indicated that with limited motor activity regulation of calcium transport in the nephron changes selectively.

It should be noted that increased activity of the ionized calcium after load was pronounced in hypokinesia to a lesser degree than under conditions of normal motor activity (Figure 2). Consequently the filtration charge of calcium in test with calcium load also rose to a lesser degree; the rate of calcium reabsorption in this case, in contrast to the sample in the background period was reduced (see Figure 2). Consequently, a more significant increase in calciumuresis in the test with load of calcium lactate under conditions of hypokinesia was governed by the more pronounced decrease of its tubular reabsorption.

Apparently with limited motor activity, there is a change in hormonal regulation of calcium transport in the renal canaliculi. Increase in secretion of parathyroid hormone, stimulating the generation in the gastrointestinal tract of gastrin [16] probably increases pro- /708
duction of calcitonin. These hormones have different-directed effect on calcium metabolism; under conditions of hypokinesia there is a dominance in the kidneys and gastrointestinal tract of the effect of

calcitonin, and in the osseous tissue, parathyroid hormone.

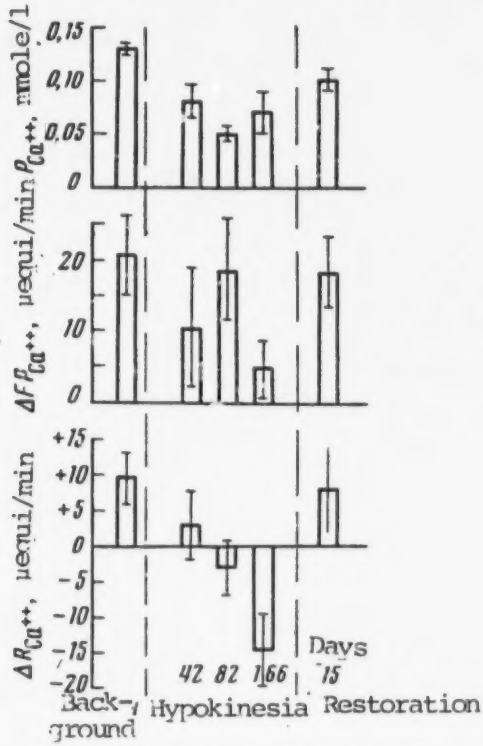

Figure 2. Increased Activity of Ionized Calcium ($\Delta P_{Ca^{++}}$) in Blood Serum, Change in Filtered Load ($\Delta FP_{Ca^{++}}$) and Rate of Calcium Reabsorption ($\Delta R_{Ca^{++}}$) in the Period of its Maximum Release in a Test with Calcium Load During 182-day Antiorthostatic Hypokinesia (M±mt)

The primary link in the genesis of changes in the metabolism of calcium under conditions of hypokinesia is apparently increased resorption of osseous tissue because of increased secretion of the parathyroid hormone, which leads to increased content of calcium ions in the blood serum. Increased generation of calcitonin is a secondary response reaction of the body aimed at reducing the level of ionized calcium in the blood. However on the background of dominance in processes of

metabolism of the osseous tissue, there is no decreased level of ionized calcium in the blood serum. Increased secretion of calcium by the kidneys and its reduced absorption in the gastrointestinal tract leads to permanent losses of calcium during hypokinesia.

Conclusions /709

1. When man stays under conditions of 182-day antiorthostatic hypokinesia, there is increased activity of calcium ions in the blood serum. The concentration of total calcium in the blood changed to a lesser degree.

2. The content of parathyroid hormone in blood plasma during the entire period of hypokinesia and in the beginning of restoration significantly exceeded the background level.

3. Increased excretion of calcium with urine with prolonged limited motor activity was linked not only to increased filtration charge of calcium, but also its decreased reabsorption in the renal canaliculi.

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